

Appl. No. 09/578,587
Amdt. dated Nov. 12, 2003
Reply to final Office Action of July 15, 2003

Attorney's Docket No.:103809-540NP

REMARKS

Claims 4, 6, and 11-16 are currently pending. Among them, claims 4 and 12 are allowed (the Office Action, page 4, line 7-8), and claims 6, 11, and 13-16 are rejected (the Office Action, pages 2-3). Reconsideration of this application is respectfully requested in view of the remarks below.

Rejection under 35 U.S.C. § 102(e)

Claim 11 is rejected under 35 USC § 102(e) as being anticipated by US Patent No. 5,403,728 to Jekkel *et al.*

Claim 11 is drawn to a process for obtaining mevinolin by culturing a fungal culture medium of *Aspergillus* strain. The process consists essentially of four steps: (a) adjusting the pH of a culture medium to between about 7.5 and about 10, (b) separating the culture medium from the *Aspergillus* strain, (c) adjusting the pH of the separated culture medium to between about 4.5 and about 1, and (d) recovering the mevinolin. Note that mevinolin is a compound in its lactone form, i.e., not in its dihydroxy acid form. See Examples 2-6, in which mevinolin was obtained in 98.7% to 99.7% purity and dihydromevinolin was in the range of 0.15% to 0.25%.

Jekkel *et al.* teaches a process including the steps of cultivating *Aspergillus* strain in a medium, removing the resulting fungal mycelium from the medium, recovering mevinolin and dihydromevinolin from the medium, and separating mevinolin and dihydromevinolin by anion exchange chromatography (col. 12, lines 16-56).

According to the Examiner, Jekkel *et al.* discloses that "the treatment of biomass of *A. obscurus* MV-1 to obtain mevinolin is first treated with 2N NaOH, which would be expected to yield at a pH of about 7.5 to 10, and then with sulfuric acid at a pH of about 1.5, which is within the range of 4.5 and 1" (the Office Action, page 2, paragraph 8, lines 2-5). Applicants respectfully disagree. Jekkel *et al.* only teaches treating a culture medium with 2N NaOH (having a pH of 14.3), but does not teach adjusting the pH of a culture medium, let alone adjusting pH to a range of 7.5 to 10. It is well known to a skilled person in the art that the treatment of 2N NaOH yields a basic solution having a pH in a range of 7 to 14.3, i.e., a broader range than the range of 7.5 to 10 recited in claim 11. "If the claims are directed to a narrow

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range, the reference teaches a broad range, and there is evidence of unexpected results within the claimed narrow range ... it may be reasonable to conclude that the narrow range is not disclosed with 'sufficient specificity' to constitute an anticipation of the claims ..." See the Manual of Patent Examining Procedure ("MPEP"), § 2131.03. A declaration under 37 CFR § 1.132 by Dr. Kalman Polya ("Dr. Polya's declaration," filed during prosecution), presented unexpected results obtained from a process, in which the pH of a culture medium was adjusted to about 9, i.e., a pH within the claimed narrow range. Given the unexpected results, it is reasonable to conclude that the claim narrow range (a range of 7.5 to 10) is not disclosed with "sufficient specificity" to constitute an anticipation of claim 11. MPEP, § 2131.03

More importantly, Applicants would like to bring the Examiner's attention to the transitional phrase recited in claim 11. The transitional phrase "consisting essentially of" limits the scope of claim 11 to the four steps "and those that do not materially affect the basic and novel characteristic(s)" of the claimed invention. *In re Herz*, 537 F.2d 549, 551-52 (CCPA 1976) (emphases original). The process described in Jekkel *et al.* requires a step of ion exchange chromatography (Jekkel *et al.* col. 7, lines 28-36) to obtain mevinolin in its lactone form. Such a step materially affects the basic and novel characteristics of the claimed invention because the claimed process can produce mevinolin in its lactone form without additional chromatography, and is, therefore not included in the process of claim 11. As a result, the process of claim 11 is different from that described in Jekkel *et al.*

For the reasons set forth above, Jekkel *et al.* does not anticipate claim 11.

Rejection under 35 U.S.C. § 103(a)

Claims 6, 11, and 13-16 are rejected under 35 U.S.C. § 103(a) as being unpatentable over Jekkel *et al.* in view of Nakamura *et al.* (*J. Antibiotics*, XLIII, 1597, 1990). Among the rejected claims, claim 11 is independent, from which claims 6 and 13-16 depend. Claim 11 will be first discussed.

Claim 11 is drawn to a process consisting essentially of four steps as discussed above.

The Examiner asserts that

"Jekkel *et al.* teaches the treatment of biomass of *A. obscurus* MV-1 to obtain mevinolin first with 2N NaOH, which would be expected to yield at a pH of about 7.5 to 10, and then with sulfuric acid at a pH of about 1.5. The reference differs

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from the claimed invention in that the reference does not teach the precise pH values and additives recited.

However, Nakamura *et al.* teaches ... adjusting the pH first to 10 and then to 3, which is within the range of the claimed process (See, e.g., page 1597)

Consequently, it would have been obvious to one having ordinary skill in the art at the time the claimed invention was made to modify the process of Jekkel *et al.* by modifying the pH and additives, as suggested by the teachings of Nakamura *et al.* for a process for the recovery of mevinolin ..." (the Office Action, page 3, lines 7-26).

Applicants would like to point out that both Jekkel *et al.* and Nakamura *et al.* require a step of ion exchange chromatography (Jekkel *et al.*, col. 7, lines 28-36 and Nakamura *et al.*, page 1597) to obtain mevinolin or its derivative in its lactone form, while the process of claim 11 does not include such a step. "Note that the omission of an element and retention of its function is an indicia of unobviousness" (emphasis original). See MPEP, § 2144.04IIB. The process of claim 11 omits of the step of ion exchange chromatography and retains of the function of obtaining mevinolin. Accordingly, the omission is an indicia of unobviousness. Thus, the Examiner has not met her burden of establishing a *prima facie* case of obviousness against claim 11, relying on Jekkel *et al.* and Nakamura *et al.*

Even if a *prima facie* case of obviousness has been made, it can be successfully rebutted by unexpected results provided in Dr. Polya's declaration.

More specifically, Dr. Polya's declaration shows two side-by-side preparations of mevinolin, one carried out according to Example 1 in Jekkel *et al.* and the other carried out according to the process of claim 11. The latter includes a step of adjusting the pH of a culture medium to 9. The results demonstrate that the mevinolin obtained from the process of claim 11 had fewer contaminants than the mevinolin obtained from the process described in Example 1 in Jekkel *et al.* A skilled person in the art would have not expected that by including a step of adjusting the pH of a culture medium, one could have obtained mevinolin in higher purity.

For the reasons set forth above, claim 11 is not obvious over Jekkel *et al.* and Nakamura *et al.*

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Claims 6 and 13-16, which depend from claim 11, are also not obvious in view of Jekkel *et al.* and Nakamura *et al.*, since “[d]ependent claims are nonobvious under section 103 if the independent claims from which they depend are nonobvious.” *In re Fine*, 5 USPQ2d, 1586-1600 (Fed. Cir. 1988).

CONCLUSION

Based on the foregoing amendments and remarks, favorable consideration and allowance of all of the claims now present in the application are respectfully requested.

Should the Examiner require or consider it advisable that the specification, claims and/or drawings be further amended or corrected in formal respects in order to place the case in condition for final allowance, then it is respectfully requested that such amendment or correction be carried out by Examiner's Amendment and the case passed to issue. Alternatively, should the Examiner feel that a personal discussion might be helpful in advancing this case to allowance, the Examiner is invited to telephone the undersigned.

The Commissioner is authorized to charge any required fees, including any extension and/or excess claim fees, any additional fees, or credit any overpayment, to Goodwin Procter LLP Deposit Account No. 06-0923.

Respectfully submitted,



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